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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/403,440	01/19/2000	DAVID PHILIP LANE	MEWB25.001AP	7276

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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 01/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/403,440	LANE, DAVID PHILIP	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *5-10, 12-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Accordingly, group I, claims 1-4, 11, species "a peptide having a sequence corresponding to human p53" and species "treatment of cancer" are examined in the instant application.

This application contains claims drawn to an invention nonelected with traverse in Paper 09/30/03. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

The following are the remaining rejections.

INTERVIEW REQUEST

The request for an interview in paper of 09/30/03 is acknowleged. However, due to the presence of many complex, unsolved issues, this Office action is set forth. Applicant is invited to consider this Office action. An interview will be granted upon request, if still deemed necessary.

RESTRICTION

Applicant asserts that the present application are unified by the feature that the methods are applied to cells in which mdm2 is not overexpressed. Applicant asserts that by ignoring the fact that the claims are all limited to cells which do not overexpress

mdm2, the Examiner has ignored the very feature that distinguishes the present invention from the prior art.

Applicant further asserts that the species peptide FxaaXaaXaaW carries all the limitations of the first one, i.e a peptide having a sequence corresponding to human p53.

Applicant's arguments in paper of 09/30/03 have been considered but are found not to be persuasive for the following reasons:

It is noted that in the original claim 1, the claimed method comprises administrating to an individual an agent having the property of disrupting the binding of p53 and mdm2. It is further noted that there is no limitation that the individual to which the agent is administered does not overexpress mdm2.

In addition, it is noted that the amendment of claim 1 in the response of 09/30/03 does not affect the restriction requirement, since the restriction requirement is based on originally presented claims.

WO 96/02642A1 teaches a method for interfering with the binding between p53 and MDM2, comprising administering an effective amount of a compound which is able to disrupt or prevent the binding between p53 and MDM2 (p.5, second paragraph). Said compound includes peptide fragments of p53, which include at least some of amino acids 18-23 of human p53, or the sequence FxxLW (p.5, last three paragraphs).

Because the method of the prior art comprises the same method steps as originally claimed in the instant invention using the same composition, i.e. administering to "an individual" "a compound which is able to disrupt or prevent the binding between

p53 and MDM2", the claimed method is anticipated because the method will inherently lead to the claimed effects. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993).

Thus unity of the claimed invention does not exist according to PCT rule 13.2, because the method is anticipated by the art.

The requirement is still deemed to be proper, and therefore made FINAL.

Accordingly, group I, claims 1-4, 11, species "a peptide having a sequence corresponding to human p53" and species "treatment of cancer" are examined in the instant application.

REJECTION UNDER 35 USC 112, SECOND PARAGRAPH, NEW REJECTION

Claims 1-4, 11 are indefinite, for using the language "inducing growth inhibition of apoptosis in a population of cells" in the amended claim 1, because it is not clear what "inducing growth inhibition of apoptosis in a population of cells" means. It is not clear how one could induce growth inhibition of apoptosis, because apoptosis or programmed cell death does not have any growth.

For the purpose of compact prosecution, it is assumed that claim 1 is drawn to a method for inducing growth inhibition or apoptosis in a population of cells in which mdm2 is not overexpressed, comprising administering an agent that disrupts the binding of p53 and mdm2.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, NEW MATTER, NEW REJECTION

Claims 3-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 3-4 are drawn to a method for inducing growth inhibition or apoptosis in a population of cells in which mdm2 is not overexpressed, comprising administering an agent that disrupts the binding of p53 and mdm2, wherein said agent comprises a peptide having an amino acid sequence that "consists of" a variant or a portion of human p53, which has the property of binding to mdm2.

A review of the specification reveals that the specification has support for p53 peptides of less than 25, 20 or 15 amino acids, and variant peptides of p53, which include the motif FxxxW (p.7, second paragragph)

The specification however does not disclose a method for inducing growth inhibition or apoptosis in a population of cells in which mdm2 is not overexpressed, comprising administering an agent that disrupts the binding of p53 and mdm2, wherein said agent comprises a peptide having an amino acid sequence that "consists of" "a variant or a portion of human p53", which has the property of binding to mdm2.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT

Claims 1-4, 11 remain rejected under 35 USC 112, first paragraph pertaining to lack of enablement for a method for inducing growth inhibition or apoptosis in cells in

which mdm2 is not overexpressed or in cancer cells, for reasons already of record in paper No:17.

Applicant asserts that the claimed invention is based on finding a new class of situations, in which one would want to disrupt the binding of p53 and mdm2, and that known ways of doing so may be used.

Applicant asserts that the claims have now been amended to avoid explicit reference to in vivo methods, thereby rendering the issue moot.

Applicant argues that US patents have been granted that are equivalent to WO93/20238 and WO 96/02642, to which the present application refers extensively. Applicant argues that US patents 6,153,391, which is equivalent to WO 96/02642 creates the presumption that the patent meets the statutory enablement requirement. Applicant argues that the present disclosure which provides an equivalent teaching should be accepted as enabling for the same reasons.

Applicant's arguments in paper of 09/30/03 have been considered but are found not to be persuasive for the following reasons:

It is noted that different applications are different and the patenting of US 6,153,391 does not apply to the instant application.

Further, the treated cells in the present application are not the same as the treated cells in US 6,153,391,having different characteristics and properties, i.e. cells that do not overexpress mdm2 versus cells that overexpress mdm2.

The claims read on a method for inducing growth inhibition or apoptosis in vitro or in vivo in a population of cells in which mdm2 is not overexpressed, including cancer cells.

One cannot extrapolate from increased transcriptional activity of p53 in transfected breast tumor cells with growth inhibition or apoptosis of a population of cells in which mdm2 is not overexpressed, or cancer cells in which mdm2 is not overexpressed, because the particular cellular outcome in response to activated p53 depends on cell type, cellular context and extracellular signals, and that in some cases p-53 mediated apoptosis can be inhibited by the presence of survival factors, including various cytokines, as taught by Haupt et al, of record. The specification however does not disclose that the cell type that do not overexpress mdm2 have growth inhibition or apoptosis in response to activation of p53. In view of the teaching of Haupt et al, one cannot predict that cells that do not overexpress mdm2 have growth inhibition or apoptosis in the presence of an agent that disrupts the binding of p53 and mdm2.

Further, one cannot extrapolate from increased transcriptional activity of p53 in transfected breast tumor cells with **in vivo** growth inhibition or apoptosis of a population of cells in which mdm2 is not overexpressed, or cancer cells in which mdm2 is not overexpressed, because in vitro conditions cannot be extrapolated to in vivo conditions, and because characteristics of cultured cell lines are different from primary cancer cells, as taught by Drexler et al, Embleton et al, Hsu et al, Freshney et al, and Dermer, all of record, and because cancer treatment is unpredictable, as taught by Gura et al, Jain et al, Curti et al, and Hartwell et al, all of record.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE

1. Claims 1-4, 11 remain rejected under 35 USC 112, first paragraph pertaining to **lack of enablement for** a method for inducing growth inhibition or apoptosis in cells in which mdm2 is not overexpressed, which are cancer cells, comprising administering **an agent or a variant of p53, that disrupts the binding of p53 and mdm2**, for reasons already of record in paper No:17.

Claims 1-4, 11 remain rejected under 35 USC 112, first paragraph pertaining to lack of enablement for a method for inducing growth inhibition or apoptosis in cells in which mdm2 is not overexpressed or in cancer cells, for reasons already of record in paper No:17.

Applicant asserts that the claimed invention is based on finding a new class of situations, in which one would want to disrupt the binding of p53 and mdm2, and that known ways of doing so may be used.

Applicant argues that US patents have been granted that are equivalent to WO93/20238 and WO 96/02642, to which the present application refers extensively. Applicant argues that US patents 6,153,391, which is equivalent to WO 96/02642 creates the presumption that the patent meets the statutory enablement requirement. Applicant argues that the present disclosure which provides an equivalent teaching should be accepted as enabling for the same reasons.

Applicant's arguments in paper of 09/30-03 have been considered but are found not to be persuasive for the following reasons:

It is noted that different applications are different and the patenting of US 6,153,391 does not apply to the instant application.

The claims encompass a method for inducing growth inhibition or apoptosis in cells in which mdm2 is not overexpressed or in cancer cells, comprising administering an agent of any structure, such as small molecule or any variant of p53, having any structure that disrupts the binding of p53 and mdm2.

The specification and the claim do not disclose how to make such diverse molecules for use in the claimed methods.

2. Claims 1-4, 11 remain rejected under 35 USC 112, first paragraph pertaining **to lack of enablement for a method for inducing growth inhibition or apoptosis in cells in which mdm2 is not overexpressed, or cancer cells in which mdm2 is not overexpressed**, comprising administering an agent or a variant of p53, that disrupts the binding of p53 and mdm2, for reasons already of record in paper No:17.

Applicant asserts that Applicant is not claiming any cancers or cancer cells, only those that do not overexpress mdm2.

Applicant's arguments in paper of 09/30/03 have been considered but are found not to be persuasive for the following reasons:

The claims 1-4, 11, as written, encompass a method for treating normal cells, because normal cells do not overexpress mdm2, or any cancer cell that does not overexpress mdm2.

The specification however does not disclose how to induce inhibition of growth or apoptosis in normal cells or any cancer cell that do not overexpress mdm2.

The Examiner takes noted that the claimed method could not be predicted to result in growth inhibition or apoptosis in any cancer that does not overexpress mdm2, because different cancers have different etiology and characteristics, and the responses of different cancers to a therapeutic agent are not necessarily the same, i.e. unpredictable.

Further, it is not clear what the use is for treating normal cells that do not overexpress mdm2.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

MINH TAM DAVIS

January 05, 2004

SUSAN [illegible] AR, PH.D
PRIMARY EXAMINER